REMARKS

Upon entry of the foregoing amendments, claims 45-82 are pending in the application. Claims 45, 55, 56, 61, 65, 66, 67, 69, 70, 73, 74, 77, 78, 81 and 82 have been amended to clarify the inventive subject matter and bring the claims into condition for allowance.

Applicants submit that the amendments do not introduce new matter within the meaning of 35 U.S.C. § 132. Accordingly, entry of the amendments is respectfully requested.

Request for Interview

Applicants respectfully request the Examiner to grant an interview with the applicants' attorney prior to acting on this response.

1. Rejection of claims 1-70 under the doctrine of obvious-type double patenting

The Office Action states that claims 1-70 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-6 of U.S. Patent No. 5,709,883 for the following reasons:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no clear patentable line of demarcation between the issued claims and the instant claims since

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> the instant disclosure defines the active drug can be an analgesic and one skilled in the art would immediately envisage opioid analgesics as within the generic "analgesic". If applicants traverse, then applicants are respectfully requested to clearly point out why opioid analgesics would not be contained within the "analgesics" recited in the instant claims.

Applicants respectfully traverse the Examiner's rejection. To establish an obvious-type double patenting rejection, the Examiner is required to set forth the following: (a) the differences between the inventions defined by the conflicting claims (i.e., a claim in the patent compared to a claim in the application); and (b) the reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent. *See* MPEP §804. Further, the disclosure of the patent may not be used as prior art. *See Id.*

Applicants respectfully submit that the Office Action fails to clearly set forth the basis for the rejection. In particular, the Office Action fails to specify whether the rejection is based upon a "One-Way" or a "Two-way" analysis. The Office Action also fails to point out the differences between the inventions defined by the conflicting claims and the reasons why a person of ordinary skill in the art would conclude that the invention defined a claim in issue is an obvious variation of the invention defined in a claim of the patent. Moreover, the Office Action fails to cite

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specifically which of the rejected claims are being compared to which of the claims in the patent.

Furthermore, there are numerous non-obvious distinctions between the claims in question. While the claims of the present invention are directed to topical compositions for treating pain by transdermally delivering a drug through the skin and methods of using same, the claims of the patent are directed to injectible compositions containing a water soluble analgesic, opioid antagonist or agonist-antagonist drug and a method for preparing same. In particular, the presently claimed compositions require sodium hyaluronate present in amounts of about 2.0% to 3.5% by weight of the compositions and a molar ratio of sodium hyaluronate to a nonionic polymer of 1:0.5 to 4. In contrast, the patent claims are silent with regard to an amount of hyaluronic acid and specify a molar ratio of a negatively charged polymer to a nonionic polymer of 1:0.5 to 2. Moreover, the patent claims are limited to a nonionic polymer selected from the group consisting of carboxymethyl cellulose sodium, hydroxyethyl cellulose, hydroxypropyl cellulose and mixtures thereof.

With regard to the Examiner's comment that "the instant disclosure defines the active drug can be an analgesic and one skilled in the art would immediately envisage opioid analgesics as with the generic", applicants respectfully note that the patent

requires a water soluble analgesic whereas the present compositions may contain a water insoluble analgesic suitable for topical application and transdermal delivery. It would not have been obvious for a person of ordinary skill in the art to substitute a water insoluble analgesic for the water soluble analgesics of the patent.

Even if a rejected claim was found to be an obvious variation over the invention claimed in a claim of the patent, a double patenting rejection would be inappropriate because applicant could not have presented the rejected claims in the patent. It would have been improper to file the rejected claims in the issued patent because the patented invention is unrelated to the presently claimed invention in view of the various structural and functional distinctions described above.

Finally, applicants note that because claims 1-44 were canceled in the Preliminary Amendment filed on April 8, 1999, this rejection is inapplicable to those claims.

Accordingly, withdrawal of the rejection and an allowance of all claims pending in this application is respectfully requested.

2. Rejection of claims 45-70 under the doctrine of obvious-type double patenting

The Office Action states that claims 45-70 are rejected under the judicially created doctrine of obviousness-type double

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patenting over claims 1-12 of U.S. Patent No. 5,897,880 for the following reasons:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no clear patentable line of demarcation between the issued claims and the instant claims since there appears to be considerable overlap in structure. If applicants traverse, then applicants are respectfully requested to clearly point out a clear line of patentable demarcation between the respective sets of claims.

Applicants respectfully traverse the Examiner's rejection. In establishing an obvious-type double patenting rejection, the Examiner is required to set forth the elements discussed above in Section 1.

Applicants respectfully submit that the Office Action fails to clearly set forth the basis for the rejection. In particular, the Office Action fails to specify whether the rejection is based upon a "One-Way" or a "Two-way" analysis. The Office Action also fails to point out the differences between the inventions defined by the conflicting claims and the reasons why a person of ordinary skill in the art would conclude that the invention defined a claim in issue is an obvious variation of the invention defined in a claim of the patent. Moreover, the Office Action fails to cite specifically which of the rejected claims are being compared to which of the claims in the patent.

Furthermore, there are numerous non-obvious distinctions

between the claims in question. While the claims of the present invention are directed to topical compositions specifically for treating pain by transdermally delivering a drug through the skin and methods of administering said topical compositions for the purpose of treating pain, the claims of the patent are directed only to topical compositions which may or may not even contain a drug. Additionally, numerous claims of the present application are directed to osteoporosis and the pain related thereto, while the patent claims are silent with regard to osteoporosis. Moreover, the patent claims are limited to a nonionic polymer selected from the group consisting of carboxymethyl cellulose sodium, hydroxyethyl cellulose, hydroxypropyl cellulose and mixtures thereof, while the present claims may incorporate other nonionic polymers. It would not be obvious to a person of ordinary skill in the art to include a specific drug for treating pain or osteoporosis, or an alternative nonionic polymer, into the composition claimed in the patent.

Even if a rejected claim was found to be an obvious variation over the invention claimed in a claim of the patent, a double patenting rejection would be inappropriate because applicant could not have presented the rejected claims in the patent. It would have been improper to file the rejected claims in the issued patent because the patented invention is unrelated to the

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presently claimed invention in view of the various structural and functional distinctions described above. Furthermore, applicants are entitled to a new method of using the patented composition.

Accordingly, withdrawal of the rejection and an allowance of all claims pending in this application is respectfully requested.

3. Provisional rejection of claims 45-70 under the doctrine of obvious-type double patenting

The Office Action states that claims 45-70 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claim 10 of copending Serial No. 08/825,121 for the following reasons:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no clear patentable line of demarcation between claim 10 in the copending case and the subject matter covered by the instant claims since there appears to be considerable overlap in structure. Please note that the respective sets of claims both claim analgesics.

Applicants respectfully traverse the Examiner's rejection. In establishing an obvious-type double patenting rejection, the Examiner is required to set forth the elements discussed above in Section 1.

Applicants respectfully submit that the Office Action fails to clearly set forth the basis for the rejection. In particular, the Office Action fails to specify whether the rejection is based

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upon a "One-Way" or a "Two-way" analysis. The Office Action also fails to point out the differences between the inventions defined by the conflicting claims and the reasons why a person of ordinary skill in the art would conclude that the invention defined a claim in issue is an obvious variation of the invention defined in a claim of the prior application. Moreover, the Office Action fails to cite specifically which of the rejected claims are being compared to which of the claims in the prior application. Although the Examiner cites claim 10 of the prior application, there is no specific corresponding claim or claims specified in the present application.

Furthermore, there are numerous non-obvious distinctions between the claims in question. While the claims of the present invention are directed to topical compositions specifically for treating pain by transdermally delivering a drug for treating pain through the skin and methods of administering said topical compositions for the purpose of treating pain, the claims of the prior application are directed only to methods for using compositions which contain a drug for treating erectile dysfunction. It would not have been obvious to a person of ordinary skill in the art to substitute a drug for treating pain for a drug for treating erectile dysfunction. The present claims thus represent a composition which is not covered by the methods

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of the prior application.

Moreover, the claims of the prior application are limited to a nonionic polymer selected from the group consisting of hydroxyethyl cellulose, hydroxypropyl cellulose and mixtures thereof, while the present claims cover a composition which may substitute other nonionic polymers.

Even if a rejected claim was found to be an obvious variation over the invention claimed in a claim of the patent, a double patenting rejection would be inappropriate because applicant could not have presented the rejected claims in the patent. It would have been improper to file the rejected claims in the issued patent because the patented invention is unrelated to the presently claimed invention in view of the various structural and functional distinctions described above. Furthermore, applicants are entitled to a composition where the prior application claims are limited to a method.

Accordingly, withdrawal of the rejection and an allowance of all claims pending in this application is respectfully requested.

4. Provisional rejection of claims 45-70 under the doctrine of obvious-type double patenting

The Office Action states that claims 45-70 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claim 35, 38-42 and 44-52 of copending

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application Serial No. 09/004,631 for the following reasons:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no clear patentable line of demarcation between the respective claims in the copending cases because there appears to be considerable overlap in terms of the compositions set forth.

Applicants respectfully traverse the Examiner's rejection. In establishing an obvious-type double patenting rejection, the Examiner is required to set forth the elements discussed above in Section 1.

Applicants respectfully submit that the Office Action fails to clearly set forth the basis for the rejection. In particular, the Office Action fails to specify whether the rejection is based upon a "One-Way" or a "Two-way" analysis. The Office Action also fails to point out the differences between the inventions defined by the conflicting claims and the reasons why a person of ordinary skill in the art would conclude that the invention defined a claim in issue is an obvious variation of the invention defined in a claim of the patent. Moreover, the Office Action fails to cite specifically which of the rejected claims are being compared to which of the claims in the patent.

While the claims of the present invention are directed to topical compositions specifically for treating pain by transdermally delivering a drug for treating pain through the skin and methods of administering said topical compositions for the

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purpose of treating pain, the claims of the prior application are directed to compositions which contain an active therapeutic drug. Further, numerous claims of the present application are directed to osteoporosis and the pain related thereto, while the prior application claims are silent with regard to osteoporosis. Moreover, the patent claims are limited to a nonionic polymer selected from the group consisting of carboxymethyl cellulose sodium, hydroxyethyl cellulose, hydroxypropyl cellulose and mixtures thereof, while the present claims may incorporate other nonionic polymers. It would not be obvious to a person of ordinary skill in the art to include a specific drug for treating pain or osteoporosis, or an alternative nonionic polymer, into the composition claimed in the prior application.

Even if a rejected claim was found to be an obvious variation the invention claimed in a claim of the patent, a double patenting rejection would be inappropriate because applicant could not have presented the rejected claims in the patent. It would have been improper to file the rejected claims in the issued patent because the patented invention is unrelated to the presently claimed invention in view of the various structural and functional distinctions described above. Furthermore, applicants are entitled to methods of using the compositions where no methods were claimed in the prior application.

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Accordingly, withdrawal of the rejection and an allowance of all claims pending in this application is respectfully requested.

5. Rejection of claims 55, 65, 69, 73, 77, 81 and 82 under 35 U.S.C. § 112, first paragraph

The Office Action states that claims 55, 65, 69, 73, 77, 81 and 82 are rejected under 35 U.S.C. §112, first paragraph, for the following reasons:

> the specification, while being enabling for derivatives which are diclofenac sodium, diclofenac potassium, does not reasonably provide enablement for derivatives of diclofenac. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The disclosure only discloses these particular derivatives and no others. Since applicants have not defined what a derivative of diclofenac is with the exception of two specific salts of diclofenac, one skilled in the art would be forced to resort to undue experimentation in order to practice the invention as claimed.

With regard to the rejection based upon the enablement requirement, applicants respectfully submit that the foregoing amendments to claims 55, 65, 69, 73, 77, 81 and 82 obviate the grounds for the rejection. The claims have been amended to remove the phrase "or a derivative thereof" for which the Examiner asserts there is no support found in the specification. Accordingly, the removal of the phrase obviates the basis for the rejection.

In view of the foregoing remarks and amendments, applicants

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respectfully request that the Examiner reconsider and withdraw the above rejection.

6. Rejection of claims 45-70, 73, 77, 81 and 82 under 35 U.S.C. § 112, second paragraph

The Office Action states that claims 45-70, 73, 77, 81 and 82 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to distinctly claim the subject matter which applicants regard as the invention based upon the following reasons:

> The term "capable" in claims 45, 61, and 67 is a relative term which renders the claim indefinite. The term "capable" is not defined by the claim, the specification doe not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term "capable" is vague and indefinite since it appears as though the composition is capable of future intended use.
>
> In claims 55, 65, 69, 73, 77, 81 and 82, the term "derivative" is vague and indefinite since it is not clear what structures are encompassed thereby. In its broadest sense, a "derivative" could read on any molecular fragment of diclofenac however small and thus one skilled in the art would not be able to determine whether the claims are being infringed by the prior art. Further specificity or definition is deemed necessary.

With regard to a § 112, second paragraph, case law has defined two requirements under the statute: (1) that the claims set forth the subject matter that applicants regard as their

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invention; and (2) that the claims are communicated with a reasonable degree of particularity and distinctness to a person skilled in the art in light of the content of the disclosure and the teachings of the prior art. MPEP § 2171, § 2173, and § 2173.02.

Applicants respectfully submit that the foregoing amendments to claims 45, 61, and 67 obviate this rejection with respect to these claims. Claims 45, 61 and 67 have been amended to remove the term "capable" to remedy the alleged indefiniteness noted by the Examiner. Further, applicants respectfully submit that the foregoing amendments to claims 55, 65, 69, 73, 77, 81 and 82, have been amended to remove the term "derivative" to remedy the alleged vagueness and indefiniteness noted by the Examiner.

Accordingly, the claims, as amended, do reasonably apprise persons of ordinary skill in the art of the invention's scope. Therefore, applicants respectfully request that the Examiner reconsider and withdraw the rejection.

7. Rejection of claims 45-55, 57-65, and 67-69 under U.S.C. § 102(b)

The Office Action states that claims 45-55, 57-65, and 67-69 are rejected under 35 U.S.C. 102(b) as being anticipated by Sander et al., in U.S. Patent No. 5,356,629, for the following reasons:

> Sander et al. discloses a polymeric matrix which is suspended in an aqueous medium or can be diluted which

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> contains the claimed mixture of polymers. See Examples 9 and 10 which reduce to practice the claimed mixtures of polymers. Suitable drugs include antibiotics which are encompassed by the instant claims and specifically contemplated in their composition according to the patentees such as antibiotics. See column 4, lines 51 et seq. The molar ratios as well as the overall amounts fall within the ranges as claimed and thus would be immediately envisaged as the instant invention is concerned. Please note that the instant claims do not exclude the polymer particles required by the patentees. Future intended use as being capable of topical application would not distinguish over the composition of patentees since it would appear that such compositions are capable of topical application to treat pain. This position is taken because they are structurally overlapping those compositions set forth in the instant claims.

With regard to a § 102(b), case law has defined the test for anticipation to be whether each and every element as set forth is found, either expressly or inherently, in a single prior are reference. *Verdegall Bros. V. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP §2131. Further, the identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990).

Applicants respectfully traverse this rejection. The Sander et al. reference does not disclose each and every element that is recited in the present claims. Applicants' claims, as presently

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amended, are directed to a composition comprising a therapeutic drug for treating pain suspended in a polymer matrix. The claims are limited to a polymer matrix which contains sodium hyaluronate and an nonionic polymer, wherein the sodium hyaluronate is present in amounts of about 2.0% to 3.5% by weight. Further, the polymer matrix is suspended in a liquid medium. Within the polymer matrix, a negative charged polymer and a nonionic polymer are combined in approximately equal amounts, i.e., the molar ratio of the sodium hyaluronate to the nonionic polymer is about 1:0.5 to 4. Moreover, the claimed composition is in a form suitable for topical application.

In contrast, Sander et al. teach a moldable semi-solid composition, which contains biocompatible particles dispersed in a matrix, and which is designed for effecting bone repair when implanted to the bone. In particular, Sander et al. disclose compositions containing hyaluronic acid in amounts of 9% by weight, 8% by weight, 4.4% by weight and 4% by weight. See Examples 7, 8, 9 and 10. There is no disclosure of amounts less than 4% by weight. The disclosed compositions are specifically designed to achieve an adequate stiffness to enhance malleability. See column 5, lines 18-28. To achieve the essential level of stiffness, the patent teaches a composition containing high concentrations, i.e., between 64% to 94% by weight, of

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biocompatible particles in a polymer matrix, with more preferred embodiments of the invention calling for preferably between 82% to 90% by weight of biocompatible particles. See column 3, lines 38-47; See also, column 4, lines 21-30. Sander et al. do not disclose the presence of a drug for treating pain.

While the present composition claims positively recite an amount of hyaluronic acid ranging from about 2.0% to about 3.5% by weight, the Sander et al. disclosure indicates amounts of hyaluronic acid of at least 4% by weight. Further, while the present claims require a composition in a form suitable for topical administration, Sander et al. disclose a composition in a semi-solid form for implantation onto bone. Moreover, where Sander et al. are silent with regard to the presence of a drug for treating pain, applicants' claims positively recite a drug for treating pain as a limitation. Accordingly, the compositions disclosed by Sander et al. are structurally distinct from the claimed compositions.

With regard to the present method claims, applicants respectfully point out that these claims positively recite topical administration of the polymer matrix. Sander et al. only disclose implantation and do not disclose or even suggest topical administration of a substance.

In view of the above remarks, applicants respectfully submit

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that there is no disclosure in the prior art which would support a legal conclusion that the claimed inventive subject matter was anticipated, because each and every element, as set forth in the claims, is neither expressly or inherently described in the Sander et al. reference. Accordingly, applicants' respectfully request that the Examiner reconsider and withdraw the rejection, allow claims 45-55, 57-65, and 67-69.

8. Rejection of claims 45-82 under 35 U.S.C. §103(a)

The Office Action states that claims 45-82 are rejected under 35 U.S.C. §103(a) as being unpatentable over Leshchiner et al. (U.S. Patent No. 5,143,724) for the following reasons:

> Leshchiner et al. disclose biocompatible viscoelastic two-phase gel slurries wherein the first phase comprises hyaluronic acid and its salts (see column 3, lines 59-62). The second phase comprises cellulose derivatives such as carboxymethyl cellulose (CMC), hydroxypropylmethyl cellulose and hydroxyethyl cellulose (see column 4, lines 45-50). The solvent can be water. The concentration of hyaluronic acid can be from 0.15-5% by weight (see column 6, lines 60-65). Example 12 shows a composition comprising 1:1 CMC-hylan gel (see column 18, lines 31-37). It would have been within the purview of one having ordinary skill in the art at the time the invention was made to select the claimed active given the clear suggestion of generic teaching of any drug which can be used in the gels of Leshchiner et al. and thus absent a showing of superior results in a particular drug, all drugs disclosed usable in the gels are viewed as equivalent for the purposes of Leshchiner et al.

Applicants respectfully traverse this rejection for reasons

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stated herein and submit that the foregoing amendments clarify the inventive subject matter. Furthermore, the attached Declaration under 37 C.F.R. § 1.132 by Alan Drizen constitutes evidence in support of applicants' arguments regarding the differences between the cited reference and the claims at issue, as well as evidence sufficient to rebut a prima facie case of obviousness, if such a case was found to exist. In particular, the Declaration establishes the absence of enabling disclosure and the inoperability of Leshchiner et al.

The U.S. Supreme Court in *Graham v. John Deere Co.*, 148 U.S.P.Q. 459 (1966) held that non-obviousness was determined under § 103 by (1) determining the scope and content of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the art; and, (4) inquiring as to any objective evidence of nonobviousness.

A. The present inventive subject matter

The claims as presently amended are directed to a polymer matrix capable of having a therapeutic drug for treating pain suspended in the matrix, wherein the polymer matrix contains a negative charged polymer and a nonionic polymer combined in specific critical ratios. The presence of a negative charged

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polymer and a nonionic polymer combined in the recited ratios is critical to attaining a composition suitable for topical administration, as required by the present claims. See Specification, page 5, lines 21-31. Further, compositions with molar ratios outside the claimed boundaries develop various defects, such as sheering, air pockets and separation of the polymers, which compromise the stability of the compositions. The resulting compositions are unique in that they do not possess the normal tendencies of polymer solutions to sheer, form air pockets and separate into distinct layers. See Specification page 4, lines 9 through 17. This is due to that fact that the specific molar ratios stated in the present application, i.e., relatively equal ratios of a negative charged polymer to a nonionic polymer, have been found to mitigate the occurrence of such changes to the composition. See Specification page 4, lines 9 through 17.

B. The prior art

As previously stated in the Response and Amendment, dated March 9, 1999, Leshchiner et al. disclose biocompatible viscoelastic gel slurries consisting of two phases, i.e., a polymer in a liquid phase solvent, which may, or may not, be another polymer. Leshchiner et al. teach a slurry which is able to form a suspension where the polymer does not dissolve in the

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liquid phase, but is uniformly dispersed. See column 2, lines 10-12. Leshchiner et al. do not disclose stable compositions or compositions suitable for topical application. Leshchiner et al. is silent with regard to the presence of a drug for treating pain.

C. The differences between the claimed subject matter and the prior art

Applicants respectfully maintain that a prima facie case of obviousness is not established in view of the differences between applicants' inventive subject matter, as clarified in the amended claims, and the disclosure by Leshchiner et al. Applicants specifically direct the Examiner's attention to the following distinctions.

Leshchiner et al. do not specify use of specific molar ratios between polymers in order to obtain a composition suitable for topical administration. Leshchiner et al. do discuss numerous different ratios. However, none of these ratios is disclosed as having any effect upon the suitability of a substance for topical administration. Leshchiner et al. state only that an active substance "will slowly diffuse from the viscoelastic slurry after implantation into the body and the diffusion rate can be conveniently controlled by changing the compositional parameters of the slurries." See column 8, lines 60-63. In contrast, the present inventive subject matter specifically discloses a

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composition limited to a specific critical polymer ratio, which is utilized to obtain a composition for topical admininstration. By limiting the claims to a topical drug delivery composition comprising a critical ratio, said claims exclude the compositions disclosed by Leshchiner et al. Therefore, the reference is deficient in its failure to disclose or suggest effective topical compositions.

Further, the claimed compositions and methods require the presence of a drug for treating pain. Leshchiner et al. fails to disclose or suggest compositions containing a drug for treating pain.

Even if a prima facie case of obviousness were found to exist, applicants respectfully submit that it would be rebutted by applicants' discovery that the present composition has superior properties of stability and sustained drug release, while formulations made in accordance with the teachings of Leshchiner et al. are not suitable for topical administration and are not stable. Alternatively, a prima facie case of obviousness would be rebutted by the "teaching away" of Leshchiner et al. which suggests the use of crosslinked gels incapable of forming topical drug delivery systems.

In view of the above, applicants' claimed polymer matrix is not disclosed or suggested by Leshchiner et al. By disclosing

slurries not dependent on the molar ratio of negative charged to nonionic polymers, Leshchiner et al. fail to appreciate the unexpected properties of using equal mixtures of nonionic and negative charged polymers, as claimed by applicants. The fact that a claimed product is within the broad field of the prior art and one might arrive at it by selecting specific items and conditions does not render the product obvious in the absence of some directions or reasons for making such selection. *Ex parte Kuhn,* 132 USPQ 359 (POBA 1961).

Leshchiner et al. do not recognize the advantageous properties of a polymer mixture which is not a two phase suspension, or the usefulness of a specific polymer mixture unexpectedly found to store and release therapeutic drugs efficiently, efficaciously and over prolonged periods of time. Leshchiner et al. further do not recognize the topical drug delivery that is affected by utilization of relatively equal ratios of nonionic and negative charged polymers In failing to appreciate their advantages, Leshchiner et al. provide no reason or incentive for using polymer matrixes as claimed by the applicants. Thus, not only does the patent fail to provide the present inventive subject matter, but the Leshchiner et al. patent teaches away from applicants' inventive subject matter. Accordingly, withdrawal of the rejection and an allowance of all

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claims pending in this application is respectfully requested.

D. Declaration under 37 C.F.R. §1.132 by Alan Drizen rebuts prima facie case of obviousness asserted by Examiner

Even if a prima facie case of obviousness was found to exist, the applicants respectfully submit that the attached Declaration under 37 C.F.R. §1.132 by Alan Drizen constitutes evidence sufficient to rebut said prima facie case. As explained in the Declaration, Leshchiner et al. is entirely inoperable with regard to the topical and sustained delivery of therapeutic agents. In particular, the hyaluronic acid derivative disclosed by the cited reference is a crosslinked polymer which is not suitable for topical drug delivery. See Declaration, ¶¶ 6, 7 and 8.

Further, the Declaration substantiates that the compositions disclosed in Leshchiner et al. are substantially different from the presently claimed compositions from both a structural and functional perspective. For example, Leshchiner et al. do not specifically disclose sodium hyaluronate as required by the present invention, and compositions prepared in accordance with the teachings of Leshchiner et al. would not be capable of topical drug delivery. See Declaration, ¶¶ 10 and 11.

Additionally, the Declaration provides documentation of the unexpected superior properties of the present inventive subject matter with regard to topical drug delivery. See Declaration, ¶¶

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Accordingly, withdrawal of the rejection and allowance of claims 45-82 is respectfully requested.

CONCLUSION

Based upon the above remarks, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the rejections of the remaining claims, and allow all pending claims presented herein for reconsideration. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

The Examiner is welcomed to telephone the undersigned attorney if he has any questions or comments.

Respectfully submitted,

NATH & ASSOCIATES

Date: September 30, 1999

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